Roseanolone: A New Diterpene from *Hypoestes rosea*

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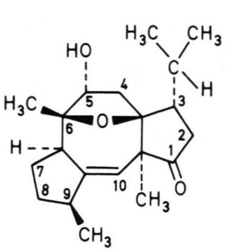
Roseanolone is a new diterpene from the African plant *Hypoestes rosea* (Acanthaceae). The isolation is described; the structure has been determined to be 1,2,3,3a,4,5,6,6a,7,8,9,10a-dodecahydro-5-hydroxy-3-isopropyl-3a, 6-oxa-6,9,10a-trimethyl-dicyclopenta[a,d] cycloocten-1-one by X-ray crystallography.

Hypoestes rosea is a shrub of the family Acanthaceae. Eventhough there is no clear reference to its use in Nigerian folk medicine, it is similar morphologically to other plants of the same family that are reported to be used in local herbal medicine and can therefore be confused with such plants. Besides this point is the fact that the chemotaxonomy of the plants of the family Acanthaceae is still not clear cut. It was therefore decided to examine systematically the extractives from plants of the family Acanthaceae that were easily available. Dried plant material was ground and extracted overnight with *n*-hexane. The gum arising upon the removal of the solvent was chromatographed on silica gel "Merck". Elution with hexane/ether mixtures gave five compounds, one of which was named roseanolone (**1**). **1** analysed for $C_{20}H_{30}O_3$, and had a molecular ion of 318 in its mass spectrum. Recrystallization from ethyl acetate/petroleum ether yielded single crystals, m.p. 170–173 °C, with $[\alpha]^{20}_{D} = +97$ °C ($c = 2.22$, $CHCl_3$).



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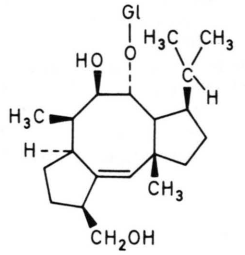

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The structure was determined by x-ray crystal structure analysis (see Fig. 1). The crystals had the space group $P2_12_12_1$, $a = 8.70(1)$, $b = 17.81(2)$, $c = 11.25(1)$ Å, $Z = 4$. The density was $1.212\ g \cdot cm^{-3}$. The crystal system was determined from Weissenberg photographs. Intensities were collected on a STOE two-circle diffractometer (Cu K_α radiation) equipped with a graphite monochromator; the crystal was oriented along *c*. 1454 reflections *h k 0* to *h k 9* with $4° \leqq 0 \leqq 60°$ were measured in the $\theta - 2\theta$ scan mode. The data were corrected for background and for Lorentz and polarization factors, but not for absorption.

The structure was solved with SHELX-77[2] by direct methods. Anisotropic refinement of the C and O atoms, and refinement of the positions of the H atoms using 1128 reflections with $(F) > 2\sigma$ reduced F to 0.082. The shift in the last least squares cycle did not exceed 0.20 of the e.s.d's. The final parameters are listed in Table I. Bond lengths and bond angles are given in Fig. 2.

The epoxydicyclopenta[a,d] cyclooctenone diterpene skeleton of roseanolone has no precedence as an extractive from higher plants. The skeleton, however, is similar to that of fusicoccin (**2**) a metabolite of microorganisms [3]. The stereochemistry, however, is quite different, and there seems to be no biogenetic relationship. Thus roseanolone is probably the first member of this new class of diterpenes reported from higher plants.

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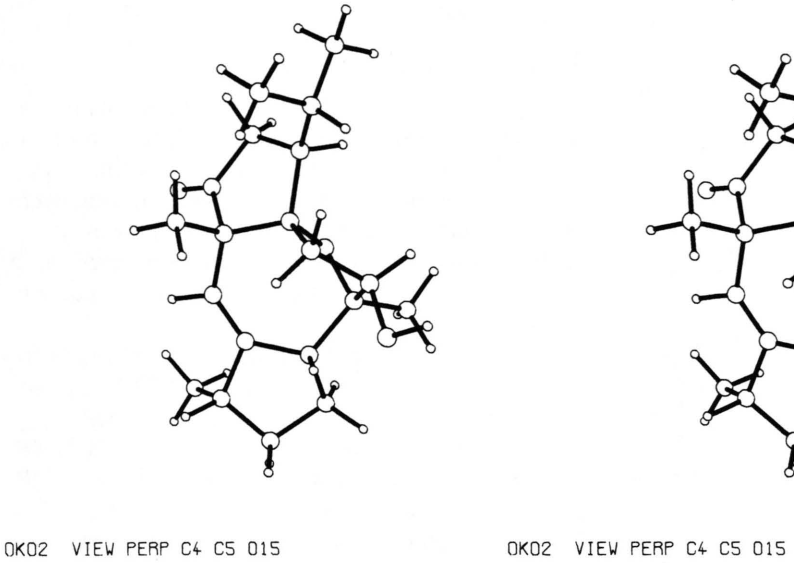

Fig. 1. Relative configuration of **1**

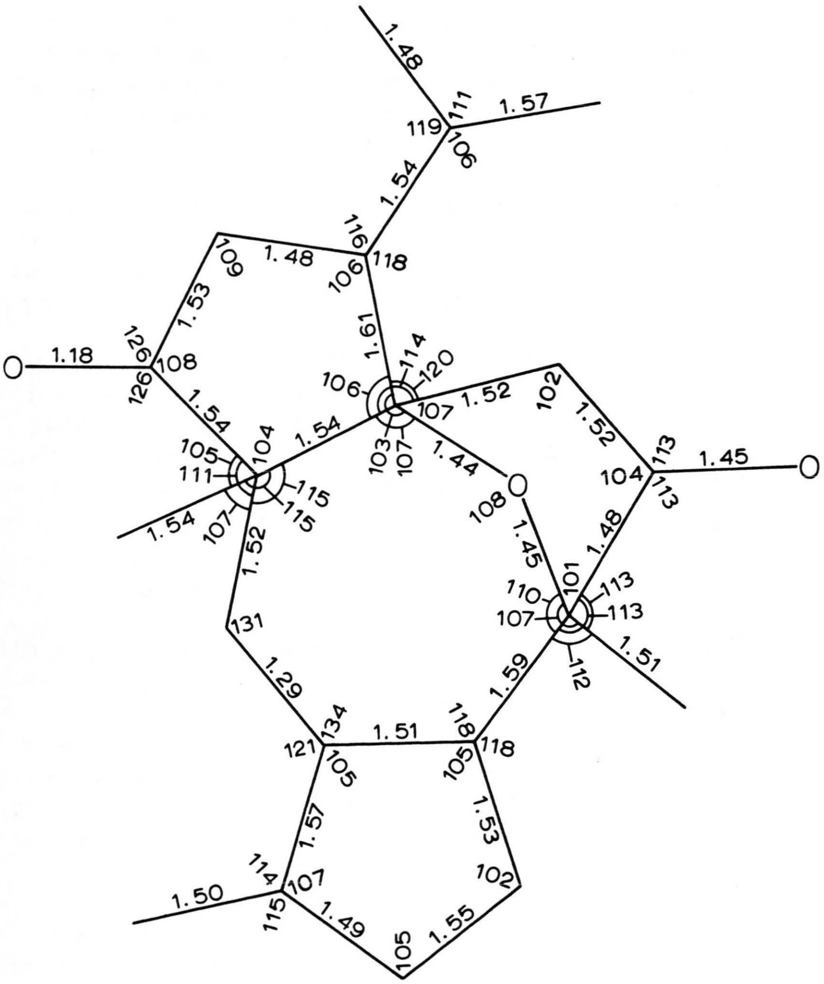

Fig. 2. Bond lengths and bond angles for **1** e.s.d.'s: $\sigma_r = 0.01$ Å, $\sigma_\alpha = 1$ °.

Table I. Structural parameters of **1** with e.s.d.'s in parentheses; a) positional parameters; b) thermal parameters Uij used in the formula $T = \exp[-2\pi^2 (U_{11} a^{*2} \cdot h^2 + \ldots + 2 U_{12} a^* \cdot b^* \cdot h k]$ for the heavy atoms, isotropic temperature factor for all hydrogen atoms: $U = 0.08$ Å²

Table I a.

ATOM	*X/A⁻*	*Y/B*	*Z/C*
C1	−0.0638(12)	−0.0642(5)	0.6567(10)
C2	−0.2172(12)	−0.0306(6)	0.6111(10)
C3	−0.1768(9)	0.0460(5)	0.5681(8)
C4	−0.0239(8)	0.0689(4)	0.6328(7)
C5	0.0440(8)	0.1316(4)	0.6083(8)
C6	0.1840(9)	0.1688(4)	0.6629(7)
C7	0.3008(9)	0.1919(4)	0.5664(7)
C8	0.4616(10)	0.1885(6)	0.6223(9)
C9	0.4530(8)	0.1469(4)	0.7356(7)
C10	0.2778(7)	0.1069(4)	0.8681(7)
C11	0.2070(9)	0.1069(4)	0.8681(7)
C12	0.2099(10)	0.0220(5)	0.8809(8)
C13	0.1856(9)	−0.0052(5)	0.7581(8)
C14	0.0132(10)	0.0041(5)	0.7148(8)
C15	0.2845(6)	0.0453(3)	0.6916(5)
C16	−0.1702(14)	0.0538(8)	0.4355(11)
C17	0.1309(10)	0.2435(5)	0.7181(9)
C18	0.2718(7)	0.2112(4)	0.4684(6)
C19	0.5252(11)	0.1856(7)	0.8450(10)
C20	0.4662(13)	0.2600(7)	0.8820(13)
C21	0.7022(11)	0.1898(8)	0.8191(12)
C22	0.0950(7)	−0.0053(4)	0.9632(6)
C23	0.2450(11)	−0.0841(5)	0.7378(10)
H11	0.005	−0.086	0.584
H12	−0.084	−0.108	0.721
H21	−0.300	−0.028	−0.682
H22	−0.263	−0.064	0.540
H3	−0.268	0.085	0.591
H5	−0.008	0.163	0.537
H81	0.503	0.245	0.639
H82	0.540	0.160	0.563
H9	0.529	0.099	0.735
H111	0.275	0.134	0.936
H112	0.091	0.128	0.871
H12	0.316	0.002	0.919
H14	−0.033	0.014	0.803
H161	−0.128	0.110	0.423
H162	−0.274	0.046	0.384
H163	−0.084	0.014	0.406
H171	0.049	0.231	0.787
H172	0.073	0.273	0.647
H173	0.220	0.279	0.754
H19	0.493	0.152	0.921
H201	0.345	0.260	0.902
H202	0.490	0.301	0.813
H203	0.530	0.274	0.961
H211	0.758	0.215	0.895
H212	0.720	0.225	0.742
H213	0.750	0.135	0.803
H22	0.144	−0.015	1.059
H231	0.176	−0.122	0.791
H232	0.361	−0.083	0.773
H233	0.247	−0.104	0.647

Experimental

Extraction of *Hypoestes rosea:*

Hypoestes rosea (11.5 kg fr. wt of whole plant) was crushed and extracted with hexane. The hexane extract (75 g) was chromatographed on alumina (1 kg). The fractions eluted with 30% ether in hexane were pooled together (27.6 g). 15 g of this was chromatographed on silica gel (300 g) subjected to a batch elution of increasing concentration of ether in hexane.

Melting points are uncorrected. IR spectra were obtained using a Perkin Elmer – 137 IR spectrophotometer and (for lupeol) using KBr pellets on Perkin Elmer – 577 IR spectrophotometer. ^{1}H-NMR spectra were determined on a Varian T60A NMR spectrometer and (for lupeol) on a Varian XL-100 NMR spectrometer. Mass spectra were determined on a Varian MAT-112S spectrometer at 70 eV. The x-ray diffraction intensities were collected on a STOE two circle diffractometer connected to a PDP-9 computer. Preparative TLC plates coated with Merck silica gel $PF_{254+366}$ and for column chromatography either Merck silica gel 60 (70–230 mesh) or activated alumina was used.

5–10% ether in hexane gave the known triterpenoid, lupeol (130 mg) which was further purified by column chromatography on silica gel and recrystallized from methanol-chloroform. m.p. 214–215 °C (l.c. [4] 216–218 °C)
IR (KBr) 3320, 3070, 2940, 2870, 1635, 1465, 1450, 1375, 1040, 880 cm^{-1} – ^{1}H-NMR ($CDCl_3$) $\delta = 0.76$ (3H, s), 0.79 (s, 3H), 0,83 (s, 3H), 0,94 (s, 3H), 0,96 (s, 3H), 1.04 (s, 3H), 1.24 (s), 1.68 (s, 3H), 3.17 (m, 1H), 4.57 (bds, 1H), 4.68 (bds, 1H) – MS (70 eV): *m/e* = 426 (36%, M^+).

$C_{30}H_{50}O$	Calculated	C 84.44	H 11.81
	Found	C 84.07	H 11.98.

The spectral data were similar to those reported [5] for lupeol and were identical with those of authentic lupeol.

The isolated compound yielded an acetate (m.p. 216–218 °C, *m/e* = 468, M^+, 19%), on treatment with acetic anhydride and pyridine overnight. The IR spectra was identical with that of the acetate which was prepared from authentic lupeol.

15% ether in hexane gave two compounds (isoroseanolone, 415 mg and roseanolone, 760 mg). Each was further purified by column chromatogra-

Table I b.

ATOM	U11	U22	U33	U23	U13	U12
C1	0.067(7)	0.037(5)	0.071(8)	0.023(5)	−0.035(6)	−0.025(5)
C2	0.057(7)	0.090(9)	0.058(8)	0.021(6)	−0.019(6)	−0.051(7)
C3	0.021(4)	0.061(6)	0.041(6)	−0.012(5)	−0.007(4)	−0.008(4)
C4	0.018(4)	0.032(4)	0.027(5)	−0.005(4)	−0.006(4)	0.003(4)
C5	0.020(4)	0.029(4)	0.040(6)	−0.008(4)	−0.009(4)	0.001(4)
C6	0.020(4)	0.028(4)	0.026(5)	−0.003(4)	−0.004(4)	−0.004(4)
C7	0.026(4)	0.027(4)	0.027(5)	0.019(4)	−0.009(4)	−0.001(4)
C8	0.024(5)	0.087(8)	0.044(7)	0.023(6)	−0.009(5)	−0.012(5)
C9	0.018(4)	0.033(4)	0.024(5)	0.009(4)	−0.001(4)	−0.008(3)
C10	0.008(3)	0.025(4)	0.024(5)	−0.004(3)	0.004(3)	−0.004(3)
C11	0.027(4)	0.029(4)	0.030(5)	−0.006(4)	−0.003(4)	−0.004(4)
C12	0.023(4)	0.045(4)	0.022(6)	0.011(4)	−0.006(4)	0.000(4)
C13	0.029(5)	0.034(5)	0.023(5)	0.008(4)	0.001(4)	−0.001(4)
C14	0.041(5)	0.037(5)	0.022(6)	0.019(4)	−0.003(4)	−0.014(4)
C15	0.019(3)	0.026(3)	0.024(4)	0.009(2)	0.005(3)	−0.003(2)
C16	0.062(8)	0.112(11)	0.091(11)	0.038(9)	−0.036(8)	−0.055(8)
C17	0.033(6)	0.027(5)	0.059(7)	−0.003(5)	0.009(5)	0.006(4)
C18	0.036(4)	0.068(5)	0.050(5)	0.024(4)	−0.002(4)	0.003(4)
C19	0.033(6)	0.081(8)	0.050(8)	−0.014(6)	0.003(5)	−0.025(6)
C20	0.056(8)	0.089(9)	0.096(11)	0.052)9)	0.012(7)	−0.037(7)
C21	0.032(6)	0.108(10)	0.077(9)	−0.016(8)	−0.003(7)	−0.026(7)
C22	0.036(4)	0.056(4)	0.029(4)	0.014(2)	0.007(3)	−0.015(4)
C23	0.037(5)	0.032(5)	0.060(7)	0.001(5)	0.004(5)	0.002(4)

phy and recrystallised from ethyl acetate-petroleum ether.

Isoroseanolone m.p. (ethyl acetate-petroleum ether) 149 − 152 °C. IR (Nujol) 3480, 1730 cm^{-1} − ^{1}H-NMR ($CDCl_3$): $\delta = 0.82 - 1.15$ (15H) − MS (70 eV) *m/e* = 318 (M^+, 5%)

$C_{20}H_{30}O_3$ Calculated C 75.43 H 9.50
Found C 75.73 H 9.84.

Roseanolone m.p. (ethyl acetate-petroleum ether) 170 − 173 °C. IR(Nujol) 3460(OH), 1730(C=O), 837 cm^{-1} ($>C=C<^{H}$) − ^{1}H-NMR($CDCl_3$): $\delta = 0.83 - 1.10$ (15H, 5CH_3), 5.20(s, 1H, $>C=C<^{\underline{H}}$) − MS (70 eV) *m/e* 318 (M^+, 13%), 300 ($M^+ - H_2O$, 7%), 159 (54%), 105 (57%), 91 (68%), 79 (53%), 55 (60%), 43 (100%).

$C_{20}H_{30}O_3$ Calculated C 75.43 H 9.50
Found C 75.25 H 9.63.

30 − 50% ether in hexane gave a crystalline compound which was purified further on TLC (developed with benzene − ethyl acetate 3:1 − R_f 0.30 − 0.35). A pure colourless crystalline compound (160 mg) was obtained. M.p. (ethyl acetate-petroleum ether) 249 − 256 °C. IR (Nujol) 1730, 1689, 1600, 1230, 948 cm^{-1} − ^{1}H-NMR ($CDCl_3$): $\delta = 1.02$ (s, 3H), 1.15 (s, 3H), 1.22 (s, 3H), 1.40 (s, 3H), 2.02 (s, 3H), 5.39 (bds, 1H), 5.64 (bds, 1H), 6.03 (s, 1H). − MS (70 eV) *m/e* 376 (M^+).

$C_{22}H_{32}O_5$ Calculated C 70.18 H 8.57
Found C 69.96 H 8.79.

70 − 80% ether in hexane gave a compound (400 mg) which was purified further by column chromatography on silica gel. m.p. (ethylacetate-petroleum ether) 223 − 230 °C. IR (Nujol) 1742, 1718, 1678, 1241, 1232, 1111, 1028, 868 cm^{-1}.

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